REMARKS

Claims 1-13 are currently pending in the application. No amendments are currently being made to the claims.

The undersigned notes the following:

1) Examiner states that "The references differ in having hydrogen instead of methyl in the position corresponding to the 4 position of applicants' formula I, e.g. ..." and then continues on to the two formulas depicted on page 3 of the Office Action. Firstly, Applicant notes that Examiner's depiction of the compounds on page 3 is incorrect and does not accurately represent the compounds utilized in the methods of the present invention, or in any of the cited references. It appears that Examiner has depicted the ethylamine chain as attached to the incorrect carbon atom. In the figures provided by the Examiner, the ethylamine chain should be attached to the carbon directly "opposite" (i.e. *para*) to the H in the first figure and directly opposite the CH_3 in the second figure.

Further, Examiner has depicted both molecules as having a CH_3 on the ethylamine chain. Applicant notes, with reference to Formula I of Furukawa, that the compounds of Furukawa do not have a CH_3 on the ethylamine chain.

2) Examiner states that "Furukawa et al teach hydroxyphenylalkylamine compounds as recited in the claims." This is incorrect. Applicant directs Examiner's attention to Formula I of the present invention. A comparison to Formula I of Furukawa in column 4 (and below) shows that Furukawa's Formula I does not have a methyl on the ethylamine side chain whereas Formula I of the present invention requires that a methyl be present at the β position of the ethylamine side chain. In short, in Furukawa, this position is an H; in the present invention, this position is CH_3. Thus, Furukawa does NOT teach hydroxyphenylalkylamine compounds "as recited in the instant claims".

Claim Rejections: 35 USC § 103(a)

Examiner has maintained the rejection of Claims 1-13 under 35 USC § 103(a) as obvious over Furukawa et al. (US 7,216,231, hereinafter "Furukawa"), Shell et al., Chiou et al, and/or Bodor et al. (hereinafter "Shell", Chiou" and "Bodor"). This rejection is again traversed.

Applicant notes that Buschmann et al (US 6,344,558), which was cited in the 103(a) rejection of the previous Office Action (mailed 08/07/2008), has not been cited in the present rejection. Applicant therefore assumes that the arguments presented in the previous response were successful in overcoming Examiner's reliance on Buschmann et al., even though Examiner did not comment on this.

In re **Wood**

In the present Office Action, Examiner again states that "the replacement of methyl with a hydrogen atom on [a] linking chain is normally within the sphere of obviousness that surrounds a known compound" and again cites in re Wood 199 USPQ 137. This position is only true some of the time and is not true as a general proposition and is not true with respect to the claimed invention. Briefly, in re Wood concerns unsubstituted vs substituted 7,7' positions of a pyrazine *ring* (in particular, a gem dialkyl substitution in a saturated ring at the 7,7 position). In contrast, the chemical group involved in the present invention is an ethylamine chain extending from a phenyl ring. Applicant reiterates that one of skill in the art would recognize that the chemistry at issue in *in re* Wood bears no similarity whatsoever to that of the compounds of the present invention, and one of skill in the art would not consider that pyrazine chemistry could be correctly applied to the compounds used in the methods currently being claimed. Further, the results of such substitutions are not necessarily obvious.

Applicant herewith files a declaration of the inventor, Dr. Richard Glennon, which confirms this argument. The declaration states that, while in some instances the substitution of, for example, methyl for H is of little consequence, in other instances, this is not the case. The substitution of methyl for H can completely alter the activity (and thus the use) of a compound. As explained in the previous response and as reiterated in the Declaration, this is the case for the compound depicted in Formula I of the present application. If R2 (position 4) of Formula I were

H instead of C_{1-3} alkyl, Cl, Br, or I, as is required by claim 1, the compound would no longer function as a serotonergic agent (i.e. a 5-HT_2 serotonin receptor agonist). Rather, if R2 was H, the compound would be an adrenergic agent, and would not longer bind to serotonin receptors. In other words, the receptor binding capability (affinity) of the compound, and hence its biological activity, changes as a result of such a substitution. Applicant notes that this is one difference between the compounds used in the methods of the present invention, and those of Shell, Chiou and Bodor, discussed further below. An additional example (Glennon et al.2000) is also discussed in the Declaration.

Furukawa as compared to the present invention

Examiner argues that "Furukawa teaches hydroxyphenylalkylamine compounds as recited in the claims...and that Shell, Chiou and Bodor all teach analogous compounds for use in treating glaucoma". As pointed out above, this is incorrect. The compounds of Furukawa are not the same as those recited in the present claims in that they do not include a methyl on the ethylamine chain. The present declaration shows that such substitutions can result in significant changes in activity of a compound, particularly when dealing with biological activity. In particular, for the compounds utilized in the methods of the present invention, the presence of the methyl advantageously confers stability against oxidative deamination.

In the previous response, Applicant described in detail additional differences between the compounds of the invention and those of the Furukawa. The compounds of the present invention contain two chiral centers, denoted α and β in formula I above. The α chiral center is created by the presence of CH_3 (instead of H).As a result, the compounds utilized in the method of the present invention exist as four optical isomers. In contrast, the compounds described by Furukawa have only one chiral center. The single chiral center is located at the position analogous to that of the "β" chiral center in the compounds of the present invention (see Formula I of claim 1). The compounds of Furukawa thus exist as only two optical isomers. In fact, Furukawa is directed to production of one or the other of these two isomers, i.e. to the production of a substantially pure enantiomeric optically active compound (see, for example, the abstract;

the first sentence of the Summary in column 3 at lines 21-23; column 18, lines 6-32; the Examples, which describe the production of optically active compounds; and claim 1, which recites "A process for producing an optically active ...derivative..."). Whereas the compounds of the present invention require two chiral centers, creation of a second chiral center in the compounds of Furukawa would nullify and render inoperative and/or destroy the invention of Furukawa, which *requires* the production of optically active compounds with a single chiral center. The methods of Furukawa could not be used to produce the compounds of the present invention and no straightforward or obvious variation of Furukawa's methods could be used to do so.

In addition, Applicant reiterates that the present application claims methods of lowering and controlling intraocular pressure and/or treating a mammal suffering from glaucoma. In fact, the novelty of the compounds that are used in the method is not at issue in the present application but rather whether or not such compounds have been used to lower and control intraocular pressure and/or to treat a mammal suffering from glaucoma. Furukawa clearly describes the compounds disclosed therein ONLY as anti-obesity or anti-diabetic agents (see the last sentence of the abstract, the first sentence of the Background, lines 12-17 of column 48 and lines 26-27 of column 50, which are the sole references to activity of any kind in Furukawa). There is no reference whatsoever to treating intraocular pressure or glaucoma, or anything other than obesity or diabetes, in Furukawa.

Shell, Chiou and Bodor as compared to Furukawa

Examiner cites the purportedly "analogous" (to Furukawa) compounds of Shell, Chiou and Bodor, which are described as glaucoma treatments, as teaching the treatment of glaucoma. However, to one of skill in the art, the compounds taught by Shell, Chiou and Bodor are not, in fact "analogous" to those of Furukawa. The ethylamine chain of Furukawa does not include a methyl group, whereas the ethylamine chains of Shell, Chiou and Bodor each contain a methyl group. Bodor differs further by having a tertiary butyl group, and Shell and Chiou in requiring a particular stereochemistry (please refer to the formulas in the respective references). As stated in

the accompanying Declaration, one of skill in the art, with knowledge of Shell, Chiou and Bodor, would not assume that the compounds of Furukawa could also be used to treat glaucoma, when no such use is described by Furukawa, when the compounds are so dissimilar, and given the fact that even small changes in the structure of a compound can have unpredictable results when used in a biological system.

Furukawa, Chiou, Shell and Bodor compared to the present invention

As shown above, one of skill in the art, with a knowledge of Chiou, Shell and Bodor, would not make the assumption that the compounds of Furukawa could be used to treat glaucoma. Applicant submits that one of skill in the art would then certainly not make the additional assumption that the compounds disclosed in the present application, which, as described above, also differ from those of Furukawa, could be used successfully in such a manner.

In addition, it is important to note that, the compounds of Shell and Chiou (which show the same compound) and Bodor differ markedly from those used in the present invention. The compounds depicted in these references are adrenergic agents whereas those of the present invention are serotonergic agents. In Shell, Chiou and Bodor, the position corresponding to R2 must be H, and in the present invention, R2 cannot be H but is C_{1-3} alkyl, Cl, Br, or I. As a result, the compounds of the present invention are serotonergic agents rather than adrenergic agents. The compounds of Shell, Chiou and Bodor thus differ markedly from those of the present invention both in chemical composition and in activity, and in and of themselves, cannot render obvious the use of the compounds of the present invention for treating glaucoma. As shown above, the compounds of Shell, Chiou and Bodor also differ from those of Furukawa as well. Thus, Applicant submits that no combination of these four references renders the present invention obvious.

In summary, the compounds described by 1) Furukawa and 2) Shell, Chiou and Bodor differ substantially from each other and both sets of compounds differ substantially from the compounds that are used in the methods of the present invention. Thus, the treatment of

glaucoma using the compounds of the present invention is not obvious in view of any of the cited references, or in view of any combination of the cited references.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of this rejection.

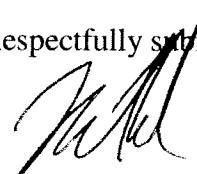
Concluding Remarks

In view of the foregoing, it is requested that the application be reconsidered, that claims 1-13 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400 (fax: 703-787-7557; email: mike@wcc-ip.com) to discuss any other changes deemed necessary in a telephonic or personal interview.

If an extension of time is required for this response to be considered as being timely filed, a conditional petition is hereby made for such extension of time. Please charge any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,



Michael E. Whitham
Reg. No. 32,635

Whitham, Curtis, Christofferson & Cook, P.C.
11491 Sunset Hills Road, Suite 340
Reston, VA 20190
703-787-9400 (Telephone)
703-787-7557 (Facsimile)

Customer No. 30,743